was tested using 2 TMAs containing 564 tissue samples. Results demonstrated that there was a significant increase in the percent of cores that stained strongly for $p27^{Kip1}$ as fixation time increased from 0 (same-day processing) to 1 or more days ($P < .001$). The authors, therefore, concluded

Brief tissue fixation to decrease diagnostic turnaround time might limit the reliability of interpretation of some forms of immunohistochemical staining.

that brief tissue fixation to decrease diagnostic turnaround time might limit the reliability of interpretation of some forms of immunohistochemical staining. In addition, and more importantly, TMAs, which assure identical test conditions, provide an excellent platform for the evaluation of the effects of tissue fixation on immunohistochemical staining.

Limitations of Tissue Microarrays in the Evaluation of Focal Alterations of bcl-2 and p53 in Whole Mount Derived Prostate Tissues

Merseburger AS, Kuczyk MA, Serth J, et al.

Oncol Rep. 2003;10:223–228.

Several investigators have reported the correlation of p53 and bcl-2 immunoreactivity with postoperative PSA recurrence.[6-8] Focal and/or clustered expression is typical for these biomarkers. The purpose of this study was to compare the effectiveness of TMAs to detect p53 and bcl-2 overexpression and their prognostic significance. TMAs of 99 patients, with a mean follow-up of 61 months, contained 760 samples from 241 carcinomas, 431 benign glands, and 88 foci of prostatic intraepithelial neoplasia (PIN). Through the use of TMA technology, overexpression of p53 and bcl-2 was detected in 43.3% and 23.7% of the patients, respectively, compared with 66.0% and 26.9% in the corresponding radical prostatectomy samples. Therefore, although TMA is regarded as a powerful tool to study the multifocal and heterogeneous nature of prostate cancer, the prognostic value of p53 and bcl-2 could not be confirmed using this technology in contrast to radical prostatectomy sections. To this end, TMA is probably more informative and reliable in evaluating the prognostic value of homogeneously expressed biomarkers.

In conclusion, TMAs have a great advantage in that numerous tissues can be investigated at the same time, which not only reduces time and cost but also assures identical test conditions for all the samples. However, the limitation of TMAs appears to be their relative inability to demonstrate heterogeneity of the tumor because of the small sample size used. ■

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Vasectomy and Prostate Cancer

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Vasectomy is the most frequently used form of male contraception in the United States, with approximately 500,000 procedures performed annually.[1] However, several case-control and cohort studies conducted over the past decade have demonstrated conflicting results regarding the possible association between vasectomy and prostate cancer risk.[2-5] This has raised considerable concern, not only among men undergoing vasectomy but also among urologists performing the procedure. Many urologists now screen for prostate cancer early in men who have had a vasectomy and even discourage vasectomy in men with a strong family history of prostate cancer.[6]

The following study further investigated the possible association between vasectomy and prostate cancer in New Zealand, which has the highest prevalence of vasectomy in the world.[7]

Vasectomy and Risk of Prostate Cancer

Cox B, Sneyd MJ, Paul C, et al.

JAMA. 2002;287:3110-3115.

The authors conducted a national population-based case-control study of 923 new cases of prostate cancer among

men aged 40 to 74 years from the New Zealand Cancer Registry who were on the general electoral roll. The control group (n = 1224) was randomly selected from the general electoral roll and matched in 5-year age groups. The primary study outcome was the relative risk (RR) of prostate cancer for men who had vasectomies compared with controls. Mean ages for the cases and controls were 66 and 65 years, respectively. All cases and controls were contacted via telephone by interviewers who were blinded to the subject group and who collected information regarding previous illnesses, urologic symptoms and surgical procedures, smoking and alcohol consumption, prostate-specific antigen testing, digital rectal examination, family history of cancer, sociodemographic characteristics, and history of vasectomy. Results demonstrated no association between prostate cancer and vasectomy (RR, 0.92; 95% confidence interval [CI], 0.71-1.14) or time since vasectomy (RR, 0.92; 95% CI, 0.68-1.23 for ≥25 years since vasectomy). Furthermore, adjustment for social class, geographic region, religious affiliation, and family history of prostate cancer did not affect the RRs. The authors concluded that vasectomy does not increase the risk of prostate cancer, even at 25 years post-procedure or longer. Despite the fact that nearly all subjects (97%) were of European descent and, as such, the results may not apply to other ethnic groups, this study provides strong evidence to exclude an association between vasectomy and prostate cancer. To this end, men undergoing vasectomy can be reassured that they will not incur an increased risk of developing prostate cancer. ■

Results demonstrated no association between prostate cancer and vasectomy or time since vasectomy.

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Endothelin-A Receptor Antagonists and Advanced Prostate Cancer

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The endothelin (ET) family consists of 3 peptides—ET-1, ET-2, and ET-3—each of which is composed of 21 amino acids. ETs are potent paracrine/autocrine factors with diverse activity, including modulation of vasomotor tone, nocioception, hormone production, cell proliferation, apoptosis, and stromal formation in a variety of tissues. These effects are predominantly mediated by the action of ET-1 on 2 G protein–coupled ET receptors: ETA and ETB.[1,2] In 1993, ET-1 was shown to be produced by benign prostatic epithelial cells and, subsequently, by prostate cancer cells and to play a role in the pathophysiology of prostate cancer progression.[3,4]

Within the setting of prostate cancer, there is also an impairment of the ET-1 degradation pathway, resulting in a local increase in the concentration of ET-1.[5] Furthermore, the expression of ETA receptors has been shown to be upregulated with prostate cancer tumor stage and grade.[6] There are a number of pathways by which the ET-1/ETA axis may promote prostate cancer progression.[4,7,8] ET-1 is mitogenic for prostate cancer cell lines in vitro and acts synergistically with other peptide growth factors.[7] ET-1 is also a mitogen for osteoblasts, the cell type that is pivotal in the hallmark osteoblastic response of bone to metastatic prostate cancer.[4,8] Selective ETA-receptor antagonists have been shown to block the proliferative effects of exogenous ET-1 in both prostate cancer cells and osteoblasts.[7,9] This observation has generated a great deal of interest in ETA-receptor antagonists for the management of advanced prostate cancer. The following recently published article reports on this subject.

Effect of Endothelin-A Receptor Blockade With Atrasentan on Tumor Progression in Men With Hormone-Refractory Prostate Cancer: A Randomized, Phase II, Placebo-Controlled Trial

Carducci MA, Padley RJ, Breul J, et al.

J Clin Oncol. 2003;21:679-689.

Carducci and colleagues evaluated the efficacy and safety of atrasentan (ABT-627), an endothelin-A receptor antago-